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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/647,924	10/31/2000	Hiroyoshi Hidaka	198323US0PCT	6890

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EXAMINER
TRAN, MY CHAU T

ART UNIT	PAPER NUMBER
1639	

DATE MAILED: 03/16/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/647,924	HIDAKA ET AL.	
	Examiner	Art Unit	
	MY-CHAU T TRAN	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on 2/9/05.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 5,6,9-12 and 14-16 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 5,6,9-12 and 14-16 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Claims

1. Applicant's amendment filed 2/09/2005 is acknowledged and entered. Claims 7, and 8 have been canceled. Claims 5, 9, and 10 have been amended.

2. Claims 3, and 13 were canceled and Claims 5, and 14 were amended by the amendment filed on 3/01/2004.

3. Claims 2, and 4 are canceled, and claims 15-16 are added by the amendment filed on 6/30/2003.

4. Claim 1 is canceled, and claims 5-14 are added by the amendment filed on 5/08/2002.

5. Claims 5, 6, 9-12, and 14-16 are pending.

Response to Amendment

6. Applicant's request for reconsideration of the finality of the rejection of the last Office action is persuasive and, therefore, the finality of that action is withdrawn.

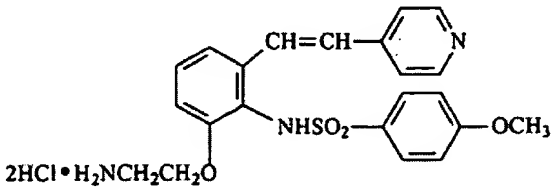
Election/Restrictions

7. Applicant has elected the following species for the elected invention (Claims 5-16):

a. A species of antigenic substance is serum albumin.

b. A species of chemical cross-linker is glutaraldehyde.

c. A species of drug is drug A, which has the following structure:



8. Claim 14 is withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to ***a nonelected species***, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper filed 8/30/02 and 10/9/02.

Priority

9. This application is a 371 of PCT/JP98/01712 filed 4/15/1998.

Withdrawn Rejection(s)

10. The rejection of claims 5-10, and 15 under 35 USC 103(a) as being obvious over Gram et al. (*Proc. Natl. Acad. Sci. USA*, **1992**, 89:3576-3580), Pecht et al. (US Patent 4,683,135), and the specification disclosure on page 3, lines 19-22, has been withdrawn in view of applicant's amendments of claim 5 and cancellation of claims 7, and 8.

11. The rejection of claims 11-12, and 16 under 35 USC 103(a) as being obvious over Gram et al. (*Proc. Natl. Acad. Sci. USA*, **1992**, 89:3576-3580) Pecht et al. (US Patent 4,683,135), and the specification disclosure on page 3, lines 19-22 as applied to claims 5-10, and 15 above, and

further in view of Barbas III et al. (*Proc. Natl. Acad. Sci. USA*, **1991**, 88:7978-7982) has been withdrawn in view of applicant's amendments of claim 5 and cancellation of claims 7, and 8.

New Rejection(s)

12. Claims 5, 6, 9-12, 15, and 16 are treated on the merit in this Office Action.

Claim Rejections - 35 USC § 112

13. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

14. Claims 5, 6, 9-12, 15, and 16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The screening step of claim 5 is vague and indefinite because it is unclear as to the metes and bounds of what is being screened, i.e. is it the protein or the labeled antibody. As claimed the screening step is to screen for the protein targeted by the drug, however the reaction being screen is antigen-antibody reaction wherein the antigen-antibody reaction is between the antigenic substance of the probe and a labeled antibody specific to the antigenic substance. Thus, there is no nexus between the labeled antibody and the protein targeted by the drug.

Claim Rejections - 35 USC § 103

15. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

16. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

17. Claims 5, 6, 9-10, and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gram et al. (*Proc. Natl. Acad. Sci. USA*, **1992**, 89:3576-3580), Odink et al. (US Patent 5,821,336, Pecht et al. (US Patent 4,683,135), and the specification disclosure on page 3, lines 19-22.

Gram et al. disclose a method for *in vitro* detection of a gene encoding a drug-targeted protein (Abstract; pg. 3578, left col., line 19 to right col. line 4). The method comprises the phage displaying low affinity Fabs binding to a progesterone-bovine serum albumin conjugate (drug-serum albumin) were isolated from the library (pg. 3578, left col., line 19 to right col. line 4; pg. 3577, left col., lines 44-62). The drug-targeted protein comprise of progesterone-bovine serum albumin wherein the progesterone bind to the bovine serum albumin via a linker comprising 3-(*O*-carboxymethyl) oxime (pg. 3577, left col., lines 47-48). The phage display comprises *Escherichia coli* (pg. 3577, left col., lines 39-43) (refers to claims 6 and 15). The

library comprises murine cDNA expression library (pg. 3577, left col., lines 1-34) (refers to claim 7). Additionally with regards to claims 8-10, the type of cDNA expression library would be a choice of experimental design and is considered within the purview of the cited prior art.

The method of Gram et al. differ from the presently claimed invention by failing to include the chemical cross-linker such as glutaraldehyde as the linker that couples the drug to the antigenic substance. However the instant specification on page 3 discloses that "*No particular limitation is imposed on the chemical cross-linkers so long as they provide a group which cross-links a functional group of the drug and a functional group of the antigenic substance*" (see specification lines 19-22). Additionally, glutaraldehyde is a known bifunctional linkers use to couple drug to an antigenic substance as disclosed by Pecht et al. Pecht et al. disclose the method of forming a drug-BSA conjugate (col. 4, lines 13-26). The method comprises using glutaraldehyde as a bifunctional reagent to couple the drug to BSA (bovine serum albumin). Thus it would be obvious to one skilled in the art to use different type of bifunctional linkers to couple the drug to an antigenic substance since the instant specification on page 3 discloses that "*No particular limitation is imposed on the chemical cross-linkers so long as they provide a group which cross-links a functional group of the drug and a functional group of the antigenic substance*" (see specification lines 19-22).

The method of Gram et al. differs from the presently claimed invention by failing to include using cDNA expression library from human cell.

Odink et al. disclose the methods for producing human polypeptides using methods of recombinant DNA technology (see e.g. col. 1, line 66 to col. 2, line 28; col. 5, lines 32-46 ; col.

6, line 2 thru col. 8, line 62). One method comprises producing cDNA expression library from human placenta cell (see e.g. col. 8, lines 14-41).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to include using cDNA expression library from human cell as taught by Odink et al. in the method of Gram et al. One of ordinary skill in the art would have been motivated to include using cDNA expression library from human cell in the method of Gram et al. for the advantage of providing polypeptides, especially human polypeptides, from the methods of recombinant DNA technology that can be use in screening for pharmaceutical compounds (Odink: col. 1, line 66 to col. 2, line 28) since both of Gram et al. and Odink et al. disclose the method of making cDNA from mRNA (Gram: pg. 3577, left col., lines 1-34; Odink: col. 8, lines 14-20). Furthermore, one of ordinary skill in the art would have reasonably expectation of success in the combination of Gram et al. and Odink et al. because Odink et al. disclose that cDNA from human cell are well known in the art (Odink: col. 7, line 57 thru col. 8, line 62).

18. Claims 11-12, and 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gram et al. (*Proc. Natl. Acad. Sci. USA*, **1992**, 89:3576-3580), Odink et al. (US Patent 5,821,336, Pecht et al. (US Patent 4,683,135), and the specification disclosure on page 3, lines 19-22 as applied to claims 5-10, and 15 above, and further in view of Barbas III et al. (*Proc. Natl. Acad. Sci. USA*, **1991**, 88:7978-7982).

Gram et al. disclose a method for *in vitro* detection of a gene encoding a drug-targeted protein (Abstract; pg. 3578, left col., line 19 to right col. line 4). The method comprises the

phage displaying low affinity Fabs binding to a progesterone-bovine serum albumin conjugate (drug-serum albumin) were isolated from the library (pg. 3578, left col., line 19 to right col. line 4; pg. 3577, left col., lines 44-62). The phage display comprises *Escherichia coli* (pg. 3577, left col., lines 39-43) (refers to claims 6 and 15). The library comprises murine cDNA expression library (pg. 3577, left col., lines 1-34) (refers to claim 7). Additionally with regards to claims 8-10, the type of cDNA expression library would be a choice of experimental design and is considered within the purview of the cited prior art. Both Gram et al. and Pecht et al. disclose using a drug-BSA conjugate to bind to an antibody (Gram: pg. 3578, right col., lines 1-4; Pecht: col. 4, lines 49-68). Gram et al. disclose drug-targeted protein comprise of progesterone-bovine serum albumin, wherein the progesterone bind to the bovine serum albumin via a linker comprising 3-(*O*-carboxymethyl)oxime.

Furthermore, the method of Gram et al. differ from the presently claimed invention by failing to include the chemical cross-linker such as glutaraldehyde as the linker that couples the drug to the antigenic substance. However the instant specification on page 3 discloses that "*No particular limitation is imposed on the chemical cross-linkers so long as they provide a group which cross-links a functional group of the drug and a functional group of the antigenic substance*" (see specification lines 19-22). Additionally, glutaraldehyde is a known bifunctional linkers use to couple drug to an antigenic substance as disclosed by Pecht et al. Pecht et al. disclose the method of forming a drug-BSA conjugate (col. 4, lines 13-26). The method comprises using glutaraldehyde as a bifunctional reagent to couple the drug to BSA (bovine serum albumin). Thus it would be obvious to one skilled in the art to use different type of

bifunctional linkers to couple the drug to an antigenic substance since the instant specification on page 3 discloses that "*No particular limitation is imposed on the chemical cross-linkers so long as they provide a group which cross-links a functional group of the drug and a functional group of the antigenic substance*" (see specification lines 19-22).

The combination of Gram et al., Odink et al., and Pecht et al. is obvious over the presently claimed invention, but the combination differ from the presently claimed invention by failing to include employing a membrane to capture phage from plated phage culture.

Barbas III et al. disclose a method of colony screening of panned libraries (pg. 7979, right col., lines 12-27). The method comprises using nitrocellulose filters (membrane) with isopropyl β-D-thiogalactopyranoside to capture the phage from plated phage culture (pg. 7979, right col., lines 12-16) (refers to claims 11-12, and 16).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to include employing a membrane to capture phage from plated phage culture as taught by Barbas III et al. in the method of Gram et al. and Pecht et al. One of ordinary skill in the art would have been motivated to include employing a membrane to capture phage from plated phage culture in the method of Gram et al. and Pecht et al. because Gram et al. incorporated the method of Barbas III et al. by reference into the disclosed colony screening method of panned libraries (Gram: pg. 3577, left col., lines 57-60). Furthermore, one of ordinary skill in the art would have reasonably expectation of success in the combination of Gram et al., Pecht et al., and Barbas III et al. because Gram et al. uses Barbas III et al. colony screening method of panned libraries (Gram: pg. 3577, left col., lines 57-60).

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to My-Chau T. Tran whose telephone number is 571-272-0810. The examiner can normally be reached on Monday: 8:00-2:30; Tuesday-Thursday: 7:30-5:00; Friday: 8:00-3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew J. Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

mct
March 11, 2005

PADMASHRI PONNALURI
PRIMARY EXAMINER